

**LISTING OF CLAIMS**

1. (Currently Amended) A solid pharmaceutical composition for the delivery of a physiologically active agent to an animal comprising:
  - a. one or more physiologically active agents in an amount effective to induce a physiological response in an animal;
  - b. one or more polysaccharides comprising subunits having anionic carboxylate or sulfate groups, and
  - c. one or more solid, polysaccharide gel inducing compositions comprising one or more pharmaceutically acceptable salts of a divalent or multivalent metal cation;wherein the pharmaceutical composition is in a ~~solid~~ powder form that forms a gel when contacted with a tissue or body fluid of an animal, and wherein the powder comprises a plurality of microparticles and/or microspheres having a particle size suitable to permit the microparticles or microspheres to pass through a sieve having an opening size of about 250  $\mu$ M in diameter.
2. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are selected from the group consisting of a pectic substance, alginate, carrageenan, and gellan.
3. (Canceled)
4. (Canceled)
5. (Canceled)
6. (Currently Amended) The solid pharmaceutical composition of claim 4 1 wherein the one or more polysaccharides comprise one or more pectins.

7. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having a degree of methylation of less than 70%.
8. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having a degree of methylation of less than 50%.
9. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having a degree of methylation of less than 25%.
10. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having a degree of methylation of less than 10%.
11. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having an average molecular weight of greater than about  $4.0 \times 10^5$  Daltons.
12. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having an average molecular weight of greater than about  $1.0 \times 10^6$  Daltons.
13. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having an average molecular weight of greater than about  $1.0 \times 10^6$  Daltons, and a degree of methylation of less than about 10%.
14. (Original) The solid pharmaceutical composition of claim 6 wherein the one or more pectins are an aloe pectin.
15. (Original) The solid pharmaceutical composition of claim 6 wherein the one or more pectins have a galacturonic acid content of greater than about 80% w/w.

16. (Original) The solid pharmaceutical composition of claim 6 wherein the one or more pectins have a rhamnose content of greater than 4% by mole.
17. (Original) The solid pharmaceutical composition of claim 1 wherein the tissue or body fluid is normal calf serum.
18. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more physiologically active agents are selected from the group consisting of a therapeutic agent, a diagnostic agent, a carbohydrate, a lipid, a peptide, a nucleic acid, a live cell, a dead cell in whole or part, a microorganism in whole or part, a virus in whole or part, a vaccine, an antigen, and a protein.
19. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more physiologically active agents comprise a peptide or a protein.
20. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more physiologically active agents comprises a vaccine.
21. (Original) The solid pharmaceutical composition of claim 20 wherein the vaccine comprises one or more antigens.
22. (Original) The solid pharmaceutical composition of claim 1 wherein the divalent or multivalent metal cation is calcium, magnesium, copper, manganese, nickel, cobalt, iron, zinc, or aluminum.
23. (Original) The solid pharmaceutical composition of claim 1 wherein the divalent or multivalent metal cation is calcium or aluminum.
24. (Original) The solid pharmaceutical composition of claim 1 wherein the pharmaceutically acceptable salt is soluble in water to the extent of at least about  $1 \times 10^{-5}$  moles per liter.

25. (Original) The solid pharmaceutical composition of claim 1 wherein the pharmaceutically acceptable salt will not dissolve in water to form a solution comprising at least  $1 \times 10^{-5}$  moles per liter.
26. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more pharmaceutically acceptable salts comprise aluminum hydroxide or calcium phosphate.
27. (Original) The solid pharmaceutical composition of claim 1 wherein the polysaccharide gel inducing composition further comprises one or more pharmaceutically acceptable excipients.
28. (Original) The solid pharmaceutical composition of claim 27 wherein the one or more pharmaceutically acceptable excipients are selected from the group consisting of binders, fillers or bulking agents, lubricants, flavors, and taste masking agents.
29. (Original) The solid pharmaceutical composition of claim 1 further comprising one or more pharmaceutically acceptable thickeners.
30. (Original) The solid pharmaceutical composition of claim 29 wherein the one or more pharmaceutically acceptable thickeners are selected from the group consisting of polyvinylpyrrolidone, carboxymethylcellulose, hydroxypropylmethylcellulose, collagen, gelatin, dextran, hyaluronic acid.
31. (Original) The solid pharmaceutical composition of claim 29 wherein the one or more pharmaceutically acceptable thickeners comprise polyvinylpyrrolidone.
32. (Currently Amended) The solid pharmaceutical composition of claim 1 wherein the one or more physiologically active agents, and the one or more polysaccharides ~~are present as a solid mixture on the molecular level~~ form a solid mixed composition phase wherein the

agent and the polysaccharide are intimately mixed on the molecular level, and the one or more solid gel inducing compositions are distinct solid phases.

33. (Original) The solid composition of claim 32 wherein the mixture on the molecular level is produced by a process of dissolving the one or more physiologically active agents, and the one or more polysaccharides in a liquid carrier, then removing the liquid carrier to produce a solid mixture on the molecular level.
34. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more physiologically active agents, the one or more polysaccharides, and the one or more solid gel inducing compositions are present as a physical mixture of separate solid components.
35. (Original) The solid pharmaceutical composition of claim 1 wherein the animal is a human.
36. (Original) A method for the sustained release of a physiologically active agent to an animal comprising administering the solid pharmaceutical composition of claim 1 to a tissue or body fluid of an animal, to form a gel in contact with the tissue or body fluids of the animal.
37. (Original) A method for the sustained release of a physiologically active agent to an animal comprising administering a liquid suspension of the solid pharmaceutical composition of claim 1, or the components thereof, to a tissue or body fluid of an animal to form a gel in contact with the tissue or body fluids of the animal.

38. (Original) The method of claim 37 wherein the tissues or body fluid of the animal are selected from the group consisting of mucosal surfaces, blood, serum, tear fluid, lung fluid, interstitial fluid, or nasal secretions.
39. (Original) The method of claim 37 wherein the animal is a human.
40. (Original) The method of claim 37 wherein the tissues or body fluids of the animal are nasal mucosal surfaces or nasal secretions.
41. (Original) The gel formed by the process of claim 37.
42. (Currently Amended) A method for the administration of a physiologically active agent to an animal comprising administering to a tissue or body fluid of an animal, ~~in any order or combination~~, the following components,
- a. one or more physiologically active agents in an amount effective to induce a physiological response in an animal;
  - b. one or more polysaccharides comprising subunits having anionic carboxylate or sulfate groups, and
  - c. one or more solid gel inducing compositions comprising one or more pharmaceutically acceptable salts of a divalent or multivalent metal cation;
- to form a gel in contact with the tissue or body fluids of the animal, wherein components a, b, and c are administered as components of a powder comprising a plurality of microparticles and/or microspheres having a particle size suitable to permit the microparticles or microspheres to pass through a sieve having an opening size of about 250  $\mu$ M in diameter.
43. (Canceled)

- 44. (Original) The method of claim 42 wherein components a and b are administered as separate or mixed powders.
- 45. (Original) The method of claim 42 wherein components a and b are administered as a mixture of one or more powders comprising component a and one or more powders comprising component b.
- 46. (Original) The method of claim 42 wherein components a and b are administered as components of a solid composition prepared by dissolving one or more physiologically active agents and one or more polysaccharides in a liquid carrier, and then removing sufficient liquid carrier to form the solid mixed composition.
- 47. (Canceled)
- 48. (Original) The method of claim 42 wherein components a and b are administered as a solution in a liquid carrier.
- 49. (Original) The method of claim 42 wherein the one or more polysaccharides comprise a pectin.
- 50. (Original) The method of claim 42 wherein the one or more physiologically active agents comprise a peptide, a protein, or a vaccine.
- 51. (Original) The method of claim 42 wherein the tissue body fluid is a nasal mucosal surface or a nasal secretion.
- 52. (Original) The method of claim 42 wherein the animal is a human.
- 53. (Currently Amended) A composition for the controlled release of a physiologically active agent to an animal comprising:

- a. one or more physiologically active agents in an amount effective to induce a physiological response in an animal; and
- b. one or more pectic substances having a degree of methylation less than about 30% and an average molecular weight of greater than about  $1 \times 10^5$  Daltons,

wherein the composition is a ~~solid~~ powder capable of forming a gel when contacted with a tissue or body fluid of an animal, and wherein the powder comprises microparticles and/or microspheres that have an particle size suitable to permit the microparticles or microspheres to pass through a sieve having an opening size of about 250  $\mu$ M in diameter.

- 54. (Canceled)
- 55. (Original) The composition of claim 53 wherein the pectic substance has a degree of methylation less than about 15%.
- 56. (Original) The composition of claim 53 wherein the pectic substance has an average molecular weight of greater than about  $5.0 \times 10^5$  Daltons.
- 57. (Original) The composition of claim 53 wherein the pectic substance has a molecular weight greater than  $1 \times 10^6$  Daltons and a degree of methylation of less than 10%.
- 58. (Original) The composition of claim 53 wherein the pectic substance has a galacturonic acid content of greater than about 90% w/w.
- 59. (Original) The composition of claim 53 wherein the pectic substance comprises 3-methoxy-rhamnose.
- 60. (Original) The composition of claim 53 wherein the pectic substance has a rhamnose content of greater than 4% by mole.



- 61. (Original) The composition of claim 53 wherein the pectic substance is an Aloe pectin.
- 62. (Original) The composition of claim 53 wherein the composition comprises about 20% water by weight, or less.
- 63. (Canceled)
- 64. (Canceled)
- 65. (Currently Amended) The composition of claim ~~65~~ 53 wherein the powder comprises at least about 80% by weight of microparticles and/or microspheres having particle sizes suitable to permit the microparticles and/or microspheres to pass through a sieve having an opening size of 100  $\mu\text{M}$  in diameter but not pass through a sieve having an opening size of about 0.1  $\mu\text{M}$  in diameter.
- 66. (Currently Amended) The composition of claim ~~64~~ 53 consisting essentially of microparticles and/or microspheres, wherein the microparticles and/or microspheres having particle sizes that permits them to pass through a sieve having an opening size of about 50  $\mu\text{M}$  in diameter but not pass through a sieve having an opening size of 10  $\mu\text{M}$  in diameter.
- 67. (Original) The composition of claim 53 wherein the solid composition comprises microspheres, wherein less than 90% of the microspheres have a diameter between 0.1 and 10  $\mu\text{M}$ .
- 68. (Original) The composition of claim 53 further comprising one or more pharmaceutically acceptable thickeners.

69. (Original) The composition of claim 68 wherein the one or more thickeners are selected from the group consisting of polyvinylpyrrolidone, carboxymethylcellulose, hydroxypropylmethylcellulose, collagen, gelatin, dextran, hyaluronic acid, or alginate.
70. (Original) The composition of claim 68 wherein the one or more thickeners comprise polyvinylpyrrolidone.
71. (Original) The composition of claim 68 wherein the thickener comprises from about 01. to about 90% of the composition by weight.
72. (Original) The composition of claim 53 wherein the one or more physiologically active agents comprise one or more pharmacologically active substances selected from the group consisting of a therapeutic agent, a diagnostic agent, a carbohydrate, a lipid, a peptide, a nucleic acid, a live cell, a dead cell in whole or part, a microorganism in whole or part, a virus in whole or part, a vaccine, an antigen, and a protein.
73. (Original) The composition of claim 53 wherein the one or more physiologically active agents comprise a therapeutic agent in an amount effective to treat a disease or disease condition in an animal.
74. (Original) The composition of claim 53 wherein the one or more physiologically active agents comprise a peptide or a protein.
75. (Original) The composition of claim 53 wherein the one or more physiologically active agents comprises a vaccine.
76. (Original) The composition of claim 75 wherein the vaccine comprises one or more antigens.

77. (Currently Amended) The composition of claim ~~75~~ 76 wherein the vaccine induces an active immune response in the animal when the composition is administered to the nasal mucosa of the animal.
78. (Currently Amended) The composition of claim 77 wherein after administration to an animal the immune response of the animal increases by more than about a factor of about 10%, as measured by the antigen specific IgA levels in the lung washings of an animal as compared to the antigen specific IgA levels obtained in a control experiment that administers a control composition that does not comprise the pectic substance.
79. (Original) The composition of claim 53 wherein, based on the weight of the composition, the physiologically active agent comprises from about 0.01 % to about 90 % of the composition.
80. (Original) The composition of claim 53 wherein the pectic substance comprises from about 0.0001% to about 99% by weight of the composition.
81. (Original) The composition of claim 53 wherein the pectic substance comprises from about 0.001% to about 50% by weight of the composition.
82. (Original) The composition of claim 53 wherein the pectic substance comprises from about 0.005% to about 20% by weight of the composition.
83. (Original) The composition of claim 53 wherein the pectic substance comprises from about 0.01 to about 10% by weight of the composition.
84. (Original) The composition of claim 53 further comprising a solid polysaccharide gel inducing agent.

85. (Original) The composition of claim 84 wherein the solid polysaccharide gel inducing agent comprises one or more pharmaceutically acceptable salts of a divalent or multivalent metal cation.
86. (Original) The composition of claim 85 wherein the divalent or multivalent metal cation is calcium, magnesium, copper, manganese, nickel, cobalt, iron, zinc, or aluminum.
87. (Original) The composition of claim 85 wherein the pharmaceutically acceptable salt can dissolve in water to form a solution comprising at least about  $1 \times 10^{-5}$  moles per liter of the salt.
88. (Original) The composition of claim 85 wherein the pharmaceutically acceptable salt is a calcium salt.
89. (Original) The composition of claim 85 wherein the pharmaceutically acceptable salt is a calcium halide salt.
90. (Original) The composition of claim 85 wherein the pharmaceutically acceptable salt is sufficiently insoluble in water so as to not be capable of dissolving in water to form a solution comprising at least  $1 \times 10^{-5}$  moles per liter of the salt.
91. (Currently Amended) The composition of claim 85 wherein the one or more pharmaceutically acceptable salts comprise aluminum hydroxide or calcium ~~phosphite~~ phosphate.
92. (Original) The composition of claim 85 wherein the one or more pharmaceutically acceptable salts comprise from about 0.1 % to about 80% (w/w) of the composition.

93. (Original) The composition of claim 85 wherein the one or more divalent or multivalent metal cation salts react with the pectic substance to crosslink the carboxylate groups of the pectic substance so as to form a gel comprising the metal cation.
94. (Original) The composition of claim 85 wherein the one or more divalent or multivalent metal cation salts induce the composition to form a gel when the composition is contacted with the tissue or body fluid of an animal.
95. (Original) The composition of claim 53 wherein the tissues or body fluids of the animal are selected from the group consisting of mucosal surfaces, blood, serum, tear fluid, lung fluid, interstitial fluid, or nasal secretions.
96. (Original) The composition of claim 53 wherein the tissues or body fluids of the animal are nasal secretions.
97. (Original) A method for the sustained release of a physiologically active agent to an animal comprising contacting the composition of claim 53 with a tissue or body fluid of the animal.
98. (Original) The method of claim 97 wherein the composition forms a gel comprising the physiologically active agent in contact with the tissues or body fluids on or after administration to the tissues or body fluids.
99. (Original) The method of claim 97 wherein the gel provides a sustained time release of the physiologically active agent to the tissues or body fluids.
100. (Original) The gel formed by the process of claim 99.
101. (Original) A method for the sustained release of a physiologically active agent to an animal comprising administering a liquid suspension of the solid pharmaceutical

composition of claim 53, or the components thereof, to a tissue or body fluid of an animal to form a gel in contact with the tissue or body fluids of the animal.

102. (Original) A method for the sustained release of a physiologically active agent to an animal comprising contacting the composition of claim 53 with an eye, a mucosal surface, or a wound of the animal.
103. (Original) A method for the sustained release of a physiologically active agent to an animal comprising contacting the composition of claim 53 with one or more bodily fluids of the animal selected from the group consisting of blood, serum, tear fluid, lung fluids, interstitial fluid, or nasal secretions.
104. (Original) A method for the sustained release of a physiologically active agent to an animal comprising administering the composition of claim 53 to the nasal mucosal surfaces and secretions of a human.
105. (Original) A method of making the composition of claim 53 comprising mixing in any sequence the physiologically active agent, the pectic substance, and one or more optional components and processing the mixture to form the solid composition.
106. (Currently Amended) The method of claim 94 105 wherein the one or more optional components comprise a thickener.
107. (Currently Amended) The method of claim 94 105 wherein the one or more optional components comprise a polyvinyl pyrrolidone.
108. (Currently Amended) The method of claim 94 105 wherein the physiologically active agent and the pectic substance are dissolved in a liquid carrier, then the volatile components of the liquid carrier are removed to form the solid composition.

109. (Currently Amended) The method of claim 94 105 wherein the physiologically active agent, the pectic substance, and any optional components are solids and are mixed and processed as solids.
110. (Currently Amended) The method of claim 94 105 wherein the optional component comprises a solid gel inducing agent comprising one or more pharmaceutically acceptable salts of a divalent or multivalent metal cation.
111. (Currently Amended) A method for administering a vaccine to an animal, comprising administering to ~~the mucosal surfaces of the animal~~ the animal's mucosal surfaces:
- a. one or more powders comprising microspheres or microparticles that have an particle size suitable to permit the microparticles or microspheres to pass through a sieve having an opening size of about 250  $\mu$ M in diameter, and that separately or together comprise
    - i) a pectic substance having a degree of methylation less than about 30% and an average molecular weight of greater than  $1 \times 10^5$  Daltons, in an amount effective to form a gel when the composition is contacted with the mucosal surfaces of an animal;
    - ii) one or more antigens selected from the group consisting of a peptide, a protein, a nucleic acid, a live cell, a dead cell or a portion thereof, or a virus, in an amount that is capable of inducing an active immune response in the animal; and
  - b. administering the powder to the nasal tissues and/or nasal fluids of the animal to form a gel in contact with the tissues or body fluids, and

- c. inducing an active immune response to one or more of the antigens in the animal.
112. (Original) The solid pharmaceutical composition of claim 1 wherein the one or more polysaccharides are a pectin having an average molecular weight of greater than about  $1.0 \times 10^5$  Daltons.